

WHAT IS CLAIMED:

1. A multi-arm block copolymer useful as a drug delivery vehicle, comprising a central core molecule comprising a residue of a polyol, and at least three copolymer arms
5 covalently attached to the central core molecule, each copolymer arm comprising an inner hydrophobic polymer segment covalently attached to the central core molecule and an outer hydrophilic polymer segment covalently attached to the hydrophobic polymer segment, wherein the central core molecule and the hydrophobic polymer segment define a hydrophobic core region, and wherein the hydrophobic polymer segment comprises a
10 poly(hydroxyester).
2. The multi-arm block copolymer of Claim 1, wherein the central core molecule is a residue of a polyol comprising 3 to about 25 hydroxyl groups.
- 15 3. The multi-arm block copolymer of Claim 2, wherein the central core molecule is a residue of a polyol comprising 3 to about 8 hydroxyl groups.
4. The multi-arm block copolymer of Claim 2, wherein the central core molecule is a residue of a polyol selected from the group consisting of glycerol, hexaglycerol,
20 sorbitol, pentaerythritol, and hydroxypropyl- β -cyclodextrin.
5. The multi-arm block copolymer of Claim 1, wherein the inner hydrophobic polymer segment comprises a poly(hydroxyester) selected from the group consisting of poly(lactide), poly(glycolide), poly(lactide)/(glycolide) copolymer, poly(butylolactide),
25 and polycaprolactone.
6. The multi-arm block copolymer of Claim 1, wherein the outer hydrophilic polymer segment comprises poly(ethylene glycol).

7. The multi-arm block copolymer of Claim 1, wherein each hydrophobic and hydrophilic polymer segment has a molecular weight of about 500 Da to about 100,000 Da.

5 8. The multi-arm block copolymer of Claim 1, wherein each hydrophobic polymer segment has a molecular weight of about 10,000 Da to about 40,000 Da.

9. The multi-arm block copolymer of Claim 1, wherein each hydrophilic polymer segment has a molecular weight of about 1,000 Da to about 20,000 Da.

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10. The multi-arm block copolymer of Claim 1, wherein the central core molecule is attached to at least 5 copolymer arms.

11. The multi-arm block copolymer of Claim 1, wherein the central core
15 molecule is attached to at least 8 copolymer arms.

12. The multi-arm copolymer of Claim 1, wherein the central core molecule is attached to 3 to about 8 copolymer arms.

20 13. The multi-arm block copolymer of Claim 1, wherein at least one targeting moiety is covalently attached to at least one hydrophilic polymer segment.

14. The multi-arm block copolymer of Claim 13, wherein the targeting moiety is selected from the group consisting of a protein, an antibody, an antibody fragment, a
25 peptide, a carbohydrate, a lipid, an oligonucleotide, DNA, RNA, and a small molecule having molecular weight less than 2000 Daltons.

15. The multi-arm block copolymer of Claim 13, wherein the targeting moiety is a bisphosphonate.

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16. The multi-arm block copolymer of Claim 1, wherein at least one capping group or functional group is covalently attached to at least one hydrophilic polymer segment.

5 17. The multi-arm block copolymer of Claim 16, wherein the capping group or functional group is selected from the group consisting of alkoxy, hydroxyl, protected hydroxyl, active ester, active carbonate, acetal, aldehyde, aldehyde hydrate, alkyl or aryl sulfonate, halide, disulfide, alkenyl, acrylate, methacrylate, acrylamide, active sulfone, amine, protected amine, hydrazide, protected hydrazide, thiol, protected thiol, carboxylic
10 acid, protected carboxylic acid, isocyanate, isothiocyanate, maleimide, vinylsulfone, dithiopyridine, vinylpyridine, iodoacetamide, epoxide, glyoxal, dione, mesylate, tosylate, and tresylate.

18. The multi-arm block copolymer of Claim 1, having the structure:
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$$A(-O-B-O-C-D)_n$$

wherein:

A is a central core molecule comprising a residue of a polyol,

O is oxygen,

B is a hydrophobic polymer segment comprising a poly(hydroxyester),

20 C is a hydrophilic polymer segment,

D is a capping group or functional group,

and n is 3 to about 25.

19. The multi-arm block copolymer of Claim 18, wherein each D is alkoxy.
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20. The multi-arm block copolymer of Claim 18, wherein each D is hydroxy.

21. The multi-arm block copolymer of Claim 18, wherein each D is selected from the group consisting of alkoxy, hydroxyl, protected hydroxyl, active ester, active
30 carbonate, acetal, aldehyde, aldehyde hydrate, alkyl or aryl sulfonate, halide, disulfide, alkenyl, acrylate, methacrylate, acrylamide, active sulfone, amine, protected amine,

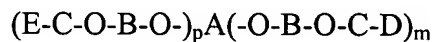
hydrazide, protected hydrazide, thiol, protected thiol, carboxylic acid, protected carboxylic acid, isocyanate, isothiocyanate, maleimide, vinylsulfone, dithiopyridine, vinylpyridine, iodoacetamide, epoxide, glyoxal, dione, mesylate, tosylate, and tresylate.

5 22. The multi-arm block copolymer of Claim 18, wherein A is a residue of a polyol selected from the group consisting of glycerol, hexaglycerol, sorbitol, pentaerythritol, and hydroxypropyl-β-cyclodextrin.

 23. The multi-arm block copolymer of Claim 18, wherein at least one of B and C
10 comprises at least one degradable linkage.

 24. The multi-arm block copolymer of Claim 18, wherein C comprises poly(ethylene glycol).

15 25. The multi-arm block copolymer of Claim 1, having the structure:



wherein:

A is a central core molecule moiety comprising a residue of a polyol,

O is oxygen,

20 B is a hydrophobic polymer segment comprising a poly(hydroxyester),

C is a hydrophilic polymer segment,

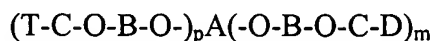
D is a hydroxyl or alkoxy group,

p is at least 1,

the sum of m and p is from 3 to about 25, and

25 E is a functional group selected from the group consisting of active ester, active carbonate, acetal, aldehyde, aldehyde hydrate, alkyl or aryl sulfonate, halide, disulfide, alkenyl, acrylate, methacrylate, acrylamide, active sulfone, amine, protected amine, hydrazide, protected hydrazide, thiol, protected thiol, carboxylic acid, protected carboxylic acid, isocyanate, isothiocyanate, maleimide, vinylsulfone, dithiopyridine,
30 vinylpyridine, iodoacetamide, epoxide, glyoxal, dione, mesylate, tosylate, and tresylate.

26. The multi-arm block copolymer of Claim 1, having the structure:



wherein:

A is a central core molecule moiety comprising a residue of a polyol,

5 O is oxygen,

B is a hydrophobic polymer segment comprising a poly(hydroxyester),

C is a hydrophilic polymer segment,

D is a capping group,

p is at least 1,

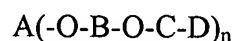
10 the sum of m and p is from 3 to about 25, and

T is a targeting moiety.

27. The multi-arm block copolymer of Claim 26, wherein T is selected from the group consisting of a protein, an antibody, an antibody fragment, a peptide, a
15 carbohydrate, a lipid, an oligonucleotide, DNA, RNA, and a small molecule having molecular weight less than 2000 Daltons.

28. The multi-arm block copolymer of Claim 26, wherein T is a bisphosphonate.

20 29. The multi-arm block copolymer of Claim 1, having the structure:



wherein:

A is a central core molecule comprising a residue of a polyol having 3 to about 8 hydroxyl groups,

25 O is oxygen,

B is a hydrophobic polymer segment comprising a poly(hydroxyester),

C is a hydrophilic polymer segment comprising poly(ethylene glycol),

D is a capping group or functional group,

and n is 3 to about 8.

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30. The multi-arm block copolymer of Claim 29, wherein each D is alkoxy or hydroxyl.

31. The multi-arm block copolymer of Claim 29, wherein A is a residue of a polyol selected from the group consisting of glycerol, hexaglycerol, sorbitol, and pentaerythritol.

32. The multi-arm block copolymer of Claim 29, wherein at least one of B and C comprises at least one degradable linkage.

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33. A multi-arm block copolymer useful as a drug delivery vehicle, comprising a central core molecule comprising a residue of a polyol having at least 3 hydroxyl groups, and at least three copolymer arms covalently attached to the central core molecule, each copolymer arm comprising an inner hydrophobic polymer segment covalently attached to the central core molecule and an outer hydrophilic polymer segment covalently attached to the hydrophobic polymer segment, wherein the central core molecule and the hydrophobic polymer segment define a hydrophobic core region, and wherein the hydrophobic polymer segment is a poly(hydroxyester) and the hydrophilic polymer segment is poly(ethylene glycol).

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34. The multi-arm block copolymer of Claim 33, wherein the central core molecule is a residue of a polyol comprising 3 to about 8 hydroxyl groups.

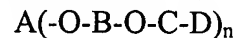
35. The multi-arm block copolymer of Claim 34, wherein the central core molecule is a residue of a polyol selected from the group consisting of glycerol, hexaglycerol, sorbitol, and pentaerythritol.

36. The multi-arm block copolymer of Claim 33, wherein the inner hydrophobic polymer segment is a poly(hydroxyester) selected from the group consisting of poly(lactide), poly(glycolide), poly(lactide)/(glycolide) copolymer, poly(butylolactide), and polycaprolactone.

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37. A multi-arm block copolymer useful as a drug delivery vehicle, comprising a central core molecule comprising a residue of a polyol having 3 to about 8 hydroxyl groups, and 3 to about 8 copolymer arms covalently attached to the central core molecule, each copolymer arm comprising an inner hydrophobic polymer segment covalently attached to the central core molecule and an outer hydrophilic polymer segment covalently attached to the hydrophobic polymer segment, wherein the central core molecule and the hydrophobic polymer segment define a hydrophobic core region, and wherein the hydrophobic polymer segment is a poly(hydroxyester) having a number average molecular weight of about 500 Da to about 40,000 Da and the hydrophilic polymer segment is a linear or branched poly(ethylene glycol) having a number average molecular weight of about 500 Da to about 100,000 Da.

38. The multi-arm block copolymer of Claim 37, having the structure:



wherein:

A is a central core molecule comprising a residue of a polyol having 3 to about 8 hydroxyl groups,

O is oxygen,

B is a poly(hydroxyester) having a number average molecular weight of about 500 Da to about 40,000 Da,

C is a linear or branched poly(ethylene glycol) having a number average molecular weight of about 500 Da to about 100,000 Da,

D is alkoxy or hydroxyl,

and n is 3 to about 8.